SEQUENCE LISTING

<110> OUIMET et al.

$<\!120\!>$ Novel membrane-bound metalloprotease NEP II and the use thereof screening inhibitors useful in therapy	for
<130> P06910US0/BAS	
<140> <141>	
<150> PCT/FR99/00807 <151> 1999-04-07	
<150> FR/9804389 <151> 1998-04-08	
<160> 29	
<170> PatentIn Ver. 2.1 <210> 1 <211> 2765 <212> DNA <213> Rattus rattus	
<220> <221> CDS <222> (107) (2428) <400> 1	
gcaaagcact agcttcagtg tgctcaaggc atccaagctc cagctgcctc cctcctggcc	60
ctggccctgg gtgctcagct gtgtgccttc cacccagaac cggctg atg ggg aag Met Gly Lys	115
tcg gag agc tca gtg ggg atg atg gag aga gcg gac aac tgt ggg agg Ser Glu Ser Ser Val Gly Met Met Glu Arg Ala Asp Asn Cys Gly Arg 5 10 15	163
agg cgc cta ggc ttc gtg gag tgt ggg ctg ctg gta ctg ctg aca ctg Arg Arg Leu Gly Phe Val Glu Cys Gly Leu Leu Val Leu Leu Thr Leu 20 25 30 35	211
ctg ttg atg gga gcc ata gtg act ctg ggt gtc ttc tac agc ata ggg Leu Leu Met Gly Ala Ile Val Thr Leu Gly Val Phe Tyr Ser Ile Gly 40 45 50	259
aag cag ctg ccc ctc tta aat agc ctg ctg cac gtc tcc cgg cat gag Lys Gln Leu Pro Leu Leu Asn Ser Leu Leu His Val Ser Arg His Glu 55 60 65	307

					-1												•
Arg	Thr	Val 70	Val	Lys	Arg	Val	Leu 75	Arg	Asp	Ser	Ser	Gln 80	Lys	Ser	Asp		
		act Thr															403
		gac Asp															451
		ggc Gly															499
		gtc Val															547
		ctg Leu 150		-			_	_		_		-			_		595
		aca Thr										Val				•	643
aga Arg 180		tct Ser									Met						691
		gcc Ala															739
		cgg Arg															787
		gac Asp 230															835
		tac Tyr															883
		aag Lys															931
		tca Ser															979°
		gat Asp															1027

295 300 305

		1	•										•		
								ccc Pro							1075
								ctg Leu							1123
								ctc Leu					tct Ser 355		1171
								aat Asn							1219
				Glu				gag Glu 380							1267
						Leu		tgģ Trp							1315
·								gaa Glu							1363
								gaa Glu					gtc Val. 435		1411
								agt Ser					atc Ile		1459
	-	 			-	-	_	aag Lys 460	-	-	-				1507
						Phe		gat Asp						. 13	1555
								gcc Ala							1603
								tac Tyr							1651
								ctg Leu							1699

					cag Gln										1747
					aag Lys										1795
					ttc Phe										1843
					cag Gln 585										1891
					ğgc Gly										1939
			_	Asp	aac Asn				-	_			_		1987
					aac Asn	Phe								·	2035
-	_	_			cag Gln		_				-	-	-		2083
	Gln				gga Gly 665										2131
					cag Gln									•	2179
					cag Gln										2227
					aac Asn										2275
					cag Gln										2323
					ggc Gly 745										2371

gcg ttc cac tgc cca cga ggc agc ccc atg cac cct atg aat cga tgt Ala Phe His Cys Pro Arg Gly Ser Pro Met His Pro Met Asn Arg Cys 760 765 770	2419
cgc atc tgg tagccaaggc tgagctatgc tgcggcccac gccccgccac Arg Ile Trp	2468
ccagaggctt cgtgaatggt gtagccggca tagatgtgca ggttgttgcc tgaaggccac	2528
tggagccacc agccagccct ccgcgcccag cctagagggc agccacccgc ccacatctgg	2588
gatgagtggt ggtgcctggt cctgcgcctt ttccggccag tgagggtcag cggcccggta	2648
ggagcagtca gctgtccccc accctcttca tagtgtgtgg ctaaatgtcc tcgagcttca	2708
gacttgagct aagtaaacgc ttcaaagaag gcaaaaaaaa aaaaaaaaa aaaaggg	2765

<210> 2 <211> 774 <212> PRT <213> Rattus rattus

<400> 2

Met Gly Lys Ser Glu Ser Ser Val Gly Met Met Glu Arg Ala Asp Asn 1 5 10 15

Cys Gly Arg Arg Leu Gly Phe Val Glu Cys Gly Leu Leu Val Leu 20 25 30

Leu Thr Leu Leu Met Gly Ala Ile Val Thr Leu Gly Val Phe Tyr 35 40 45

Ser Ile Gly Lys Gln Leu Pro Leu Leu Asn Ser Leu Leu His Val Ser 50 55 60

Arg His Glu Arg Thr Val Val Lys Arg Val Leu Arg Asp Ser Ser Gln 65 70 75 80

Lys Ser Asp Ile Cys Thr Thr Pro Ser Cys Val Ile Ala Ala Arg 85 90 95

Ile Leu Gln Asn Met Asp Gln Ser Lys Lys Pro Cys Asp Asn Phe Tyr 100 105 110

Gln Tyr Ala Cys Gly Gly Trp Leu Arg His His Val Ile Pro Glu Thr 115 120 125

Asn Ser Arg Tyr Ser Val Phe Asp Ile Leu Arg Asp Glu Leu Glu Val 130 135 140

Ile Leu Lys Gly Val Leu Glu Asp Ser Ser Val Gln His Arg Pro Ala 145 150 155 160

Val Glu Lys Ala Lys Thr Leu Tyr Arg Ser Cys Met Asn Gln Ser Val

165 170 175

Ile	Glu	Lys	Arg 180	Asp	Ser	Glu	Pro	Leu 185	Leu	Asn	Val	Leu	Asp 190	Met	Ile
Gly	Gly	Trp 195	Pro	Val	Ala	Met	Asp 200	Lys	Trp	Asn	Glu	Thr 205	Met	Gly	Pro
Lys	Trp 210	Glu	Leu	Glu	Arg	Gln 215	Leu	Ala	Val	Leu	Asn 220	Ser	Gln	Phe	Asn
Arg 225	Arg	Val	Leu	Ile	Asp 230	Leu	Phe	Ile	Trp	Asn 235	Asp	Asp	Gln	Asn	Ser 240
Ser	Arg	His	Val	Ile 245	Tyr	Ile	Asp	Gln	Pro 250	Thr	Leu	Gly	Met	Pro 255	Ser
Arg	Glu	Tyr	Tyr 260	Phe	Lys	Glu	Asp	Ser 265	His	Arg	Val	Arg	Glu 270	Ala	Tyr
Leu.	Gln	Phe 275	Met	Thr	Ser	Val	Ala 280	Thr	Met	Leu	Arg	Arg 285	Asp	Leu	Asn
Leu	Pro 290	Gly ·	Glu	Thr	Asp	Leu 295	Val	Gln	Glu	Glu	Met 300	Ala	Gln	Val	Leu
His 305	Leu	Glu	Thr	His	Leu 310	Ala	Asn	Ala	Thr	Val 315.	Pro	Gln	Glu	Lys	Arg 320
His	Asp	Val	Thr	Ala 325	Leu	Tyr	His	Arg	Met 330	Gly	Leu	Glu	Glu	Leu 335	Gln
Glu	Arg	Phe	Gly 340	Leu	Lys	Gly	Phe	Asn 345	Trp	Thr	Leu	Phe	11e 350	Gln	Asn
Val	Leu	Ser 355	Ser	Val	Gln	Val	Glu 360	Leu	Leu	Pro	Asn	Glu 365	Glu	Val	Val
Val	Tyr 370	Gly	Ile	Pro	Tyr	Leu 375	Glu	Asn	Leu	Glu	Glu 380	Ile	Ile	Asp	Val
385					390					395				Val	400
Asp	Arg	Ile	Gly	Ser 405	Leu	Ser	Gln	Arg	Phe 410	Lys	Glu	Ala	Arg	Val 415	
Tyr	Arg	Lys	Ala 420	Leu	Tyr	Gly	Thr	Thr 425	Met	Glu	Glu	Val	Arg 430	Trp	Arg
		435					440					445		Gly	
	450					455					460			Val	
Glu	Len	Tle	Glu	T.vc	Tle	Ara	Ser	Val	Phe	Val	Asn	Asn	Len	Asp	Gli

465 470 475 480

Leu Asn Trp Met Asp Glu Glu Ser Lys Lys Ala Gln Glu Lys Ala 485 490 495

Leu Asn Ile Arg Glu Gln Ile Gly Tyr Pro Asp Tyr Ile Leu Glu Asp
500 505 510

Asn Asn Arg His Leu Asp Glu Glu Tyr Ser Ser Leu Thr Phe Ser Glu
515 520 525

Asp Leu Tyr Phe Glu Asn Gly Leu Gln Asn Leu Lys Asn Asn Ala Gln 530 540

Arg Ser Leu Lys Lys Leu Arg Glu Lys Val Asp Gln Asn Leu Trp Ile
545 550 555 560

Ile Gly Ala Ala Val Val Asn Ala Phe Tyr Ser Pro Asn Arg Asn Leu 565 570 575

Ile Val Phe Pro Ala Gly Ile Leu Gln Pro Pro Phe Phe Ser Lys Asp
580 585 590

Gln Pro Gln Ala Leu Asn Phe Gly Gly Ile Gly Met Val Ile Gly His.
595 600 605

Glu Ile Thr His Gly Phe Asp Asp Asn Gly Arg Asn Phe Asp Lys Asn
610
620

Gly Asn Met Leu Asp Trp Trp Ser Asn Phe Ser Ala Arg His Phe Arg 625 630 635 640

Gln Gln Ser Gln Cys Met Ile Tyr Gln Tyr Ser Asn Phe Ser Trp Glu 645 650 655

Leu Ala Asp Asn Gln Asn Val Asn Gly Phe Ser Thr Leu Gly Glu Asn 660 665 670

Ile Ala Asp Asn Gly Gly Val Arg Gln Ala Tyr Lys Ala Tyr Leu Gln 675 680 685

Trp Leu Ala Glu Gly Gly Arg Asp Gln Arg Leu Pro Gly Leu Asn Leu 690 695 700

Thr Tyr Ala Gln Leu Phe Phe Ile Asn Tyr Ala Gln Val Trp Cys Gly 705 710 715 720

Ser Tyr Arg Pro Glu Phe Ala Ile Gln Ser Ile Lys Thr Asp Val His
725 730 735

Ser Pro Leu Lys Tyr Arg Val Leu Gly Ser Leu Gln Asn Leu Pro Gly
740 745 750

Phe Ser Glu Ala Phe His Cys Pro Arg Gly Ser Pro Met His Pro Met , 755 760 765

Asn Arg Cys Arg Ile Trp

<211> 20 <212> DNA

<213> artificial sequence

<210> 3 <211> 327 <212> DNA <213> Homo sapiens <400> 3 gggcacgaga tcacgcacgg ctttgatgac aatggccgga acttcgacaa gaatggcaac atgatggatt ggtggagtaa cttctccacc cagcacttcc gggagcagtc agagtgcatg atctaccagt acggcaacta ctcctgggac ctggcagacg aacagaacgt gaacggattc aacaccettg gggaaaacat tgetgacaac ggaggggtge ggeaageeta taaggeetae ctcaagtgga tggcagaggg tggcaaggac cagcagctgc ccggcctgga tctcacccat gagcagetet tetteateaa etatgee <210> 4 <211> 116: <212> PRT <213> Homo sapiens <400> 4 Gly His Glu Ile Thr His Gly Phe Asp Asp Asn Gly Arg Asn Phe Asp Lys Asn Gly Asn Met Met Asp Trp Trp Ser Asn Phe Ser Thr Gln His Phe Arg Glu Gln Ser Glu Cys Met Ile Tyr Gln Tyr Gly Asn Tyr Ser Trp Asp Leu Ala Asp Glu Gln Asn Val Asn Gly Phe Asn Thr Leu Gly Glu Asn Ile Ala Asp Asn Gly Gly Val Arg Gln Ala Tyr Lys Ala Tyr. Leu Lys Trp Met Ala Glu Gly Gly Lys Asp Gln Gln Leu Pro Gly Leu Asp Leu Thr His Glu Gln Leu Phe Phe Ile Asn Tyr Ala Gln Val Trp 100. Cys Gly Cys Lys 115 <210> 5

•	<220> <223> oligonucleotide		
	<400> 5		
	tggagcggca gttggctgtg		20
	<210> 6		
	<211> 21	·	
	<212> DNA		
•	<213> artificial sequence		٠
	<220>		
	<223> oligonucleotide		
	<400> 6		
	agttcccact tggggcccat g		21
	<210> 7		
	<211> 20 <212> DNA		
_	<213> artificial sequence		
]	droiff of the second		
	<220>		
] =	<223> oligonucleotide		
= 1	<400> 7		
i	gctggaggat tectetgtee		20
1			
=	<210> 8		
•	<211> 19 <212> DNA		:
Ł	<213> artificial sequence		
1			
	<220>		
=	<223> oligonucleotide		
	<400> 8		
Ξ.	cggggatcac atggtgccg		19
	<210> 9 <211> 21		
	<211> 21 <212> DNA		•
	<213> artificial sequence		
	<220> <223> oligonucleotide		
	•		
	<400> 9		
	ctaccccaag ctgcgtgata g		21
	1010. 10		
	<210> 10 <211> 21		
	<211> 21		
	<213> artificial sequence		
	· · · · · · · · · · · · · · · · · · ·		
	<220>		
	<223> oligonucleotide		

:	<400> 10		·			
	cggcaccatg tg	atccccga g				21
	<210> 11	•		•		
	<211> 22		•			
	<212> DNA					
	<213> artific	ial sequence				
	<220>					
	<223> oligonud	cleotide				
	<400> 11	•				
	gcaaagcact age	cttcagtg tg	· ·			22
				• "		
		•	···	-		
	<210> 12					
	<211> 22	•				
	<212> DNA		•			
	<213> artific	ial sequence		•		
	<220>					
	<223> oligonud	cleotide				
	<400> 12					
	ggtcatcatt cca	agatgaag ag		•		22
		•				
	<210> 13 <211> 20					
	<211> 20 <212> DNA					
	<213> artific:	ial sequence				
	<220>				•	
	<223> oligonu	cleotide				
	· · · · · · · · · · · · · · · · · · ·	cicotiac				
	<400> 13	*	•			
	cgatgaggac gc	gcctgttg				20
	<210> 14	•				
	<211> 20					•
	<212> DNA					
	<213> artific:	ial sequence		,		
	<220>					
	<223> oligonuo	cleotide				,
	<400> 14		•		,	
	tgcaggaaag gt	ttaatcta				20
	•					20
	<210> 15		•			
	<211> 20			•		
	<212> DNA <213> artific	ial sequence			:	
	<220>	alaatid:				

4005 15	
<400> 15	20
gaacgcctca gagaagcctg	20,
(210) 16	
<210> 16	
<211> 20	
<212> DNA	
<213> artificial sequence	
<220>	
<223> oligonucleotide	
<400> 16	
atgaccagaa ctccagccgg	20
<210> 17	
<211> 21	
<212> DNA	
<213> artificial sequence	
<220>	
<223> oligonucleotide	
	•
<400> 17	
catcatgctt tttctcctgg g	21
<210> 18	
<211> 21	
<212> DNA	
<213> artificial sequence	
<220>	
<223> oligonucleotide	
<400> 18	
cccgaagttt cttgaggctc c	21
	•.
<210> 19	
<211> 19	
<212> DNA	
<213> artificial sequence	-
<220>	
<223> oligonucleotide	
<400> 19	
gatcggctac cctgactac	19
<210> 20	
<211> 19	
<212> DNA	
<213> artificial sequence	•
<220>	
<223> oligonucleotide	

<400> 20		•
gttcgccatc cagtccatc		19
<210> 21		
<211> 20		
<212> DNA <213> artificial sequence		
(213) ditilitat sequence		
<220>	•	•
<223> oligonucleotide	. 7	
<400> 21		
cgaagcctag gcgcctcctc		20
<210> 22		
<211> 24	• • • • • • • • • • • • • • • • • • • •	
<212> DNA <213> artificial sequence		
<220> <223> oligonucleotide	•	
<223> Oligonacieotide		
<400> 22		
cgagatcaca catggctttg atga		, 24
<210> 23	•	
<211> 18 <212> DNA		
<213> artificial sequence		
<220>		
<pre><220> <223> oligonucleotide</pre>		•
	· .*	
<400> 23 ggacccacac cacacctg	v	18
<210> 24 <211> 22	•	
<211> 22 <212> DNA		
<213> artificial sequence		
<220>	•	
<223> oligonucleotide		
<400> 24		
cggcctggat ctcacccatg ag		22
<210> 25		
<211> 26	•	
<212> DNA		
<213> artificial sequence	i .	
<220>	•	•
<223> oligonucleotide		
<400> 25		•
ctgactgctc ccggaagtgc tgggtg		26





```
<210> 26
<211> 18 .
<212> DNA
<213> artificial sequence
<220>
<223> oligonucleotide
<400> 26
gagcagctct tcttcatc
<210> 27
<211> 22
<212> DNA
<213> artificial sequence
<220>
<223> oligonucleotide
<400> 27
ctccaccaat ccatcatgtt gc
<210> 28
<211> 6
<212> PRT
<213> artificial sequence .
<223> protein sequence corresponding to the oligonucleotide probe SEQ ID No. 22
<400> 28
Glu Ile Thr His Phe Asp
<210> 29
<211> 6
<212> PRT
<213> artificial sequence
<220>
<223> protein sequence corresponding to the oligonucleotide probe SEQ ID No. 23
<400> 29 ...
Gln Val Trp Cys Gly Ser
```

SEQUENCE LISTING

<110> OUIMET et al.

70

<120> Novel membrane-bound metalloprotease NEP II and the use thereof for screening inhibitors useful in therapy

screening inhibitors	useful in therapy		ic ase thereof for
<130> P06910US0/BAS			
<140> <141>			
<150> PCT/FR99/00807 <151> 1999-04-07			
<150> FR/9804389 <151> 1998-04-08			
<160> 29			
<170> PatentIn Ver.	2.1		
<210> 1 <211> 2765 <212> DNA <213> Rattus rattus <220>			
<221> CDS <222> (107) (242	3)		
<400> 1 GCAAAGCACT AGCTTCAGT	G TGCTCAAGGC ATCCA	AGCTC CAGCTGCCTC	CCTCCTGGCC 60
CTGGCCCTGG GTGCTCAGC	r GTGTGCCTTC CACCO	Met 0	GGG AAG 115 Gly Lys
		1	
TCG GAG AGC TCA GTG Ser Glu Ser Ser Val			
AGG CGC CTA GGC TTC Arg Arg Leu Gly Phe 20			
CTG TTG ATG GGA GCC Leu Leu Met Gly Ala 40	lle Val Thr Leu Gl		
AAG CAG CTG CCC CTC Lys Gln Leu Pro Leu 55			His Glu
AGG ACG GTT GTA AAA Arg Thr Val Val Lys			

8.0

								ATA Ile									403
		,						TGC Cys							GCT Ala 115		451
								GTG Val									499
								GAT Asp 140									547
	Val							CAG Gln									595
								ATG Met									643
						Leu		GTC Val									691
								GAG Glu								•	739
							-	AAC Asn 220								•	787
								GAT Asp									835
								TTG Leu							TAC Tyr		883
								GTA Val								.÷. ·	931
								ÄGG Arg									979
								ATG Met 300							GAG Glu	•	1027
ACA	CAT	CTG	GCC	AAC	GCC	ACG	GTC	ccc	CAG	GAG	AAA	AGG	CAT	GAT	GTC	*	1075

						-											•
Thr	His	Leu 310	Ala	Asn	Ala	Thr	Val 315	Pro	Gln	Glu	Lys	Arg 320	His	Asp	Val		
					CGA Arg												1123
					AAC Asn 345												1171
					CTG Leu												1219
					AAT Asn											•	1267
					TAC Tyr												1315
					AGA Arg											٠.	1363
					ACC Thr 425	Met									GTC Val 435		1411
					AAC Asn												1459
					AAG Lys												1507
					GTG Val										TGG Trp		1555
					AAG Lys												1603
	Glu				TAC Tyr 505												1651
					TAC Tyr												1699
					CAG Gln												1747

535 540 545

			AAG Lys					GCT Ala	•	1795
			TTC Phe							1843
			CAG Gln 585							1891
			GGC Gly							1939
			AAC Asn							1987
		Trp	AAC Asn							2035
			CAG Gln							2083
Asn			GGA Gly 665							2131
			CAG Gln							2179
			CAG Gln							2227
			AAC Asn							2275
			CAG Gln							2323
			GGC Gly 745							2371
			CGA Arg							2419

CGC ATC TGG TAGCCAAGGC TGAGCTATGC TGCGGCCCAC GCCCCGCCAC Arg Ile Trp	2468
	.•
CCAGAGGCTT CGTGAATGGT GTAGCCGGCA TAGATGTGCA GGTTGTTGCC TGAAGGCCAC	2528
TGGAGCCACC AGCCAGCCCT CCGCGCCCAG CCTAGAGGGC AGCCACCCGC CCACATCTGG	2588
GATGAGTGGT GGTGCCTGGT CCTGCGCCTT TTCCGGCCAG TGAGGGTCAG CGGCCCGGTA	2648
GGAGCAGTCA GCTGTCCCCC ACCCTCTTCA TAGTGTGTGG CTAAATGTCC TCGAGCTTCA	2708
GACTTGAGCT AAGTAAACGC TTCAAAGAAG GCAAAAAAAA AAAAAAAAA AAAAGGG	2765

<210> 2 <211> 774 <212> PRT <213> Rattus rattus <400> 2 Met Gly Lys Ser Glu

Met Gly Lys Ser Glu Ser Ser Val Gly Met Met Glu Arg Ala Asp Asn 1 5 10 15

Cys Gly Arg Arg Leu Gly Phe Val Glu Cys Gly Leu Leu Val Leu 20 25 30

Leu Thr Leu Leu Met Gly Ala Ile Val Thr Leu Gly Val Phe Tyr 35 40 45

Ser Ile Gly Lys Gln Leu Pro Leu Leu Asn Ser Leu Leu His Val Ser 50 55 60

Arg His Glu Arg Thr Val Val Lys Arg Val Leu Arg Asp Ser Ser Gln 65 70 75 80

Lys Ser Asp Ile Cys Thr Thr Pro Ser Cys Val Ile Ala Ala Ala Arg 85 90 95

Ile Leu Gln Asn Met Asp Gln Ser Lys Lys Pro Cys Asp Asn Phe Tyr
100 105 110

Gln Tyr Ala Cys Gly Gly Trp Leu Arg His His Val Ile Pro Glu Thr 115 120 125

Asn Ser Arg Tyr Ser Val Phe Asp Ile Leu Arg Asp Glu Leu Glu Val 130 135 140

Ile Leu Lys Gly Val Leu Glu Asp Ser Ser Val Gln His Arg Pro Ala 145 150 155 160

Val Glu Lys Ala Lys Thr Leu Tyr Arg Ser Cys Met Asn Gln Ser Val 165 170 175

Ile Glu Lys Arg Asp Ser Glu Pro Leu Leu Asn Val Leu Asp Met Ile

180 185 190

Gly Gly Trp Pro Val Ala Met Asp Lys Trp Asn Glu Thr Met Gly Pro 200 Lys Trp Glu Leu Glu Arg Gln Leu Ala Val Leu Asn Ser Gln Phe Asn 220 Arg Arg Val Leu Ile Asp Leu Phe Ile Trp Asn Asp Asp Gln Asn Ser 235 Ser Arg His Val Ile Tyr Ile Asp Gln Pro Thr Leu Gly Met Pro Ser Arg Glu Tyr Tyr Phe Lys Glu Asp Ser His Arg Val Arg Glu Ala Tyr 265 Leu Gln Phe Met Thr Ser Val Ala Thr Met Leu Arg Arg Asp Leu Asn 280 Leu Pro Gly Glu Thr Asp Leu Val Gln Glu Met Ala Gln Val Leu His Leu Glu Thr His Leu Ala Asn Ala Thr Val Pro Gln Glu Lys Arg 310 315 His Asp Val Thr Ala Leu Tyr His Arg Met Gly Leu Glu Glu Leu Gln Glu Arg Phe Gly Leu Lys Gly Phe Asn Trp Thr Leu Phe Ile Gln Asn Val Leu Ser Ser Val Gln Val Glu Leu Leu Pro Asn Glu Glu Val Val 360 Val Tyr Gly Ile Pro Tyr Leu Glu Asn Leu Glu Glu Ile Ile Asp Val Phe Pro Ala Gln Thr Leu Gln Asn Tyr Leu Val Trp Arg Leu Val Leu 390 395 Asp Arg Ile Gly Ser Leu Ser Gln Arg Phe Lys Glu Ala Arg Val Asp 405 Tyr Arg Lys Ala Leu Tyr Gly Thr Thr Met Glu Glu Val Arg Trp Arg Glu Cys Val Ser Tyr Val Asn Ser Asn Met Glu Ser Ala Val Gly Ser 440 Leu Tyr Ile Lys Arg Ala Phe Ser Lys Asp Ser Lys Ser Ile Val Ser 455 450 Glu Leu Ile Glu Lys Ile Arg Ser Val Phe Val Asp Asn Leu Asp Glu 4.75

Leu Asn Trp Met Asp Glu Glu Ser Lys Lys Ala Gln Glu Lys Ala

485 490 495

Leu Asn Ile Arg Glu Gln Ile Gly Tyr Pro Asp Tyr Ile Leu Glu Asp
500 505 510

Asn Asn Arg His Leu Asp Glu Glu Tyr Ser Ser Leu Thr Phe Ser Glu 515 520 525

Asp Leu Tyr Phe Glu Asn Gly Leu Gln Asn Leu Lys Asn Asn Ala Gln 530 540

Arg Ser Leu Lys Lys Leu Arg Glu Lys Val Asp Gln Asn Leu Trp Ile 545 550 555 560

Ile Gly Ala Ala Val Val Asn Ala Phe Tyr Ser Pro Asn Arg Asn Leu 565 570 575

Ile Val Phe Pro Ala Gly Ile Leu Gln Pro Pro Phe Phe Ser Lys Asp 580 585 590

Gln Pro Gln Ala Leu Asn Phe Gly Gly Ile Gly Met Val Ile Gly His 595 600 605

Glu Ile Thr His Gly Phe Asp Asp Asn Gly Arg Asn Phe Asp Lys Asn 610 615 620

Gly Asn Met Leu Asp Trp Trp Ser Asn Phe Ser Ala Arg His Phe Arg 625 630 635 640

Gln Gln Ser Gln Cys Met Ile Tyr Gln Tyr Ser Asn Phe Ser Trp Glu 645 650 655

Leu Ala Asp Asn Gln Asn Val Asn Gly Phe Ser Thr Leu Gly Glu Asn 660 665 670

Ile Ala Asp Asn Gly Gly Val Arg Gln Ala Tyr Lys Ala Tyr Leu Gln 675 680 685

Trp Leu Ala Glu Gly Gly Arg Asp Gln Arg Leu Pro Gly Leu Asn Leu 690 695 700

Thr Tyr Ala Gln Leu Phe Phe Ile Asn Tyr Ala Gln Val Trp Cys Gly 705 710 715 720

Ser Tyr Arg Pro Glu Phe Ala Ile Gln Ser Ile Lys Thr Asp Val His
725 730 735

Ser Pro Leu Lys Tyr Arg Val Leu Gly Ser Leu Gln Asn Leu Pro Gly 740 745 750

Phe Ser Glu Ala Phe His Cys Pro Arg Gly Ser Pro Met His Pro Met 755 760 765

Asn Arg Cys Arg Ile Trp 770

<210> 3 ·

<211> 327 <212> DNA <213> Homo	sapiens											
<400> 3												
GGGCACGAGA	TCACGCAC	GG CTTT	'GATGA	C AA	rggc	CGGA	ACT	CGA	CAA (GAAT(GCAAC	
ATGATGGATT	GGTGGAGT	AA CTTC	TCCAC	C CA	GCAC:	TTCC	GGG	AGCA	GTC A	AGAG'	rgcatg	
ATCTACCAGT A												
AACACCCTTG (•	•		-								
CTCAAGTGGA	TGGCAGAG	GG TGGC	AAGGA	C CA	GCAG	CTGC	CCG(GCCT(GGA !	rctc <i>i</i>	ACCCAT	
GAGCAGCTCT	TCTTCATC	AA CTAT	GCC							·		
<210> 4											•	
<211> 116						•						
<212> PRT <213> Homo :	sapiens											
<400> 4	•											
Gly His Glu	Ile Thr	His Gl	y Phe	Asp	Asp 10	Asn	Gly	Arg	Asn	Phe 15	Asp	
Lys Asn Gly	Asn Met 20	Met As	p Trp	Trp 25	Ser	Asn	Phe	Ser	Thr 30	Gl'n	His	
Phe Arg Glu 35	Gln Ser	Glu Cy	s Met 40	Ile	Tyr	Gln	Tyr	Gly 45	Asn	Tyr	Ser	
Trp Asp Leu 50	Ala Asp	Glu Gl		_. Val	Asn ·	Gly	Phe 60	Asn	Thr	Leu	Gly	
Glu Asn Ile 65	·Ala Asp	Asn Gl 70	y Gly	Val	Arg	Gln 75	Ala	Tyr	Lys	Ala	Tyr 80	
Leu Lys Trp	Met Ala 85	Glu Gl	y Gly	Lys	Asp 90	Gln	Gln	Leu	Pro	Gly 95	Leu	
Asp Leu Thr	His Glu 100	Gln Le	u Phe	Phe 105	Ile	Asn	Tyr	Ala	Gln 110	Val	Trp	
Cys Gly Cys 115	_	٠.										
<210> 5 <211> 20 <212> DNA <213> artif: <223> oligon												
<400> 5	ርጥጥርርርጥር፡	тG	,	-						•.		

<210> 6		
<211> 21		
<212> DNA	•	
<213> artificial sequence		
<223> oligonucleotide	•	
<400> 6		
AGTTCCCACT TGGGGCCCAT G		21
		2.1
<210> 7		
<211> 20		
<211> 20 <212> DNA		
<213> artificial sequence		
<223> oligonucleotide		
<400> 7		
GCTGGAGGAT TCCTCTGTCC		20
<210> 8		
<211> 19		
<212> DNA		
<213> artificial sequence	· · · · · · · · · · · · · · · · · · ·	
<223> oligonucleotide		
<400> 8		
CGGGGATCAC ATGGTGCCG		19
<210> 9		
<211> 21	·	
<212> DNA	•	
<213> artificial sequence		
<223> oligonucleotide		
(223) Oligonacicociae		
<400> 9		
CTACCCCAAG CTGCGTGATA G	1	21
CIACCCAAG CIGCGIGAIA G		21
<010× 10		
<210> 10	•	
<211> 21	•	
<212> DNA		
<213> artificial sequence		
<223> oligonucleotide		
<400> 10		
CGGCACCATG TGATCCCCGA G		21
<210> 11		
<211> 22	,	
<212> DNA		
<213> artificial sequence		
<223> oligonucleotide		
. 3		
<400> 11		
GCAAAGCACT AGCTTCAGTG TG	.	22
<210> 12		
<210> 12 <211> 22		
<212> DNA		

	<213> artificial sequence <223> oligonucleotide		
	<400> 12		
	GGTCATCATT CCAGATGAAG AG		22
	<210> 13		
	<211> 20		
	<212> DNA		
	<213> artificial sequence		
	<223> oligonucleotide		
	<400> 13		
	CGATGAGGAC GCGCCTGTTG		20
	<210> 14		
	<211> 20		•
	<212> DNA		
	<213> artificial sequence		
ne.	<223> oligonucleotide		
e .	<400> 14		
∄ =	TGCAGGAAAG GTTTGGTCTG		20
=	1001.00121.0 0111001010		2.0
=	<210> 15		
4	<211> 20		
4	<212> DNA	•	
5	<213> artificial sequence		
նար կար մեսո մեսո ը ը ում կում գո ւ	<223> oligonucleotide		
Æ .	<400> 15		
Ī	GAACGCCTCA GAGAAGCCTG		20
=	•		
ሴመነ ዓ .መነ ነ _{ው።}	<210> 16		
! =	<211> 20		
.i	<212> DNA		
,	<213> artificial sequence		
	<223> oligonucleotide		
	<400> 16		
	ATGACCAGAA CTCCAGCCGG		20
	1010: 17	•	
	<210> 17		
	<211> 21		
	<212> DNA		
	<213> artificial sequence		
	<223> oligonucleotide		
	<400> 17		
	CATCATGCTT TTTCTCCTGG G		21
	CATCAIGCIT TITCICCIGG G	•	Z I
	<210> 18		
	<211> 21		
	<211> 21 <212> DNA		
	<213> artificial sequence		
	<223> oligopugloctido		

<400> 18		
CCCGAAGTTT CTTGAGGCTC C		21
CCCCIIICITI CITCACCCIC C		21
2010× 10		
<210> 19		
<211> 19		
<212> DNA	•	
<213> artificial sequence		
<223> oligonucleotide		
<400> 19		
GATCGGCTAC CCTGACTAC		10
GATCGGCTAC CCTGACTAC	•	19
<210> 20		
<211> 19		
<212> DNA		•
<213> artificial sequence		
<223> oligonucleotide		
12207 011904020002440		٠
<400> 20		
		1.0
GTTCGCCATC CAGTCCATC		19
·		
<210> 21		
<211> 20		
<212> DNA		•
<213> artificial sequence		
<223> oligonucleotide		
12237 Ollgonacicociae		
<400> 21	•	
		00
CGAAGCCTAG GCGCCTCCTC		20
<210> 22		
<211> 24		
<212> DNA		
<213> artificial sequence		•
<223> oligonucleotide		
<400> 22		
	24	
cgagatcaca catggctttg atga	1 24	
<210> 23		
<211> 18		
<212> DNA		
<213> artificial sequence		
<223> oligonucleotide		•
<400> 23		
ggacccacac cacacctg	18	
gyaccoacac cacacotty	10	
(010) 04		
<210> 24	•	
<211> 22		
<212> DNA		
<213> artificial sequence		
<223> oligonucleotide		
·		
<400> 24	·	
cggcctggat ctcacccatg ag	22	
COOCCIDOAL CICACCCATO AO	Z.Z.	

```
<210> 25
     <211> 26
     <212> DNA
     <213> artificial sequence
     <223> oligonucleotide
     <400> 25
     ctgactgctc ccggaagtgc tgggtg
                                                                         26
     <210> 26
     <211> 18
     <212> DNA
     <213> artificial sequence
     <223> · oligonucleotide
     <400> 26
     gagcagctct tcttcatc
                                                                         18
     <210> 27
     <211> 22
1
     <212> DNA
     <213> artificial sequence
     <223> oligonucleotide
     <400> 27
١, ا
     ctccaccaat ccatcatgtt gc
                                                                         22
ij,
<210> 28
     <211> 6
LL
     <212> PRT
N
     <213> artificial sequence.
     <223> protein sequence corresponding to the oligonucleotide probe SEQ ID No. 22
<400> 28
٥٦
     Glu Ile Thr His Phe Asp
Ŋ
     <210> 29
     <211> 6
     <212> PRT
     <213> artificial sequence
     <223> protein sequence corresponding to the oligonucleotide probe SEQ ID No. 23
     <400> 29
     Gln Val Trp Cys Gly Ser
```

1